VIA FIRST CLASS MAIL

I hereby certify that this correspondence is being deposited with the U.S. Postal Service as First Class Mail in an envelope addressed to the Commissioner of Patents and Trademarks, Washington, D.C. 20231 on April 14, 2003.

Laurie Olds

Laurie Olds

AF/1644

LUD-[redacted].3 JEL/NDH (10027207)

#13 Goiga

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Applicant	:	L. DUMOUTIER, et al.
Serial No.	:	09/751,797
Filed	:	December 29, 2000
For	:	ISOLATED NUCLEIC ACID MOLECULES WHICH ENCODE T CELL INDUCIBLE FACTORS (TIFs), THE PROTEINS ENCODED, AND USES THEREOF
Art Unit	:	1644
Examiner	:	Amy Decloux

April 14, 2003

Hon. Commissioner of Patents
and Trademarks
Washington, D.C. 20231

BRIEF ON APPEAL
(37 CFR §1.192)

This brief is submitted in support of the Notice of Appeal filed in this case shortly after March 5, 2003.

Pursuant to 37 CFR §1.192(a), three copies are submitted, as is the fee called for by 37 CFR §1.17(c). A check in the amount of $160.00 is provided. Should the amount of the check be incorrect, or if the check becomes dislodged from the Brief, applicants ask that appropriate adjustment be made to Deposit Account 500624.

The following information is provided, pursuant to 37 CFR §1.192(c).

(1) REAL PARTY IN INTEREST

The real party in interest is Ludwig Institute for Cancer Research, the assignee of the application.

(2) RELATED APPEALS AND INTERFERENCES

Appellants, Appellants' representatives, and the assignee, are aware of no other appeals or interferences which will directly affect , be directly affected by, or have a bearing on the Board's decision in the pending appeal.

(3) STATUS OF CLAIMS

Claims 1, 3, 4, 7, 8, 10, 11, 14-16, 18, 19 and 50 are pending. The rejection of all of these claims is appealed. A listing of these claims is attached.

By preliminary amendment, claims 2, 5, 6, 9, 12, 13, 17 and 20-49 were cancelled.

(4) STATUS OF AMENDMENTS

A second office action issued on December 13, 2002. 37 CFR §1.191(a) permits the filing of an appeal following a second rejection of claims. No amendments have been filed thereafter.

(5) SUMMARY OF THE INVENTION

The claimed invention relates to nucleic acid molecules which encode "T cell inducible factor" or "TIF," as well as expression vectors containing these nucleic acid molecules, and recombinant cells containing either the nucleic acid molecule or the expression vector. As is explained at page 1 of the specification, the nucleic acid molecules are upregulated by interleukin-9, and induce STAT activation.

IL-9 is a very well known molecule, as pages 4-5 of the specification show. Further, it is known that IL-9 activity is mediated by STAT factor activation (page 5).

The nucleic acid molecules of the invention are expressed when IL-9 is present, but not in its absence. See page 6.

Isolated embodiments of the invention, and how they were isolated , are described. In example 1 (page 7), a cell line was admixed with IL-9, and a cDNA library was obtained. Subtraction hybridization, a well known technique, was then applied to the library. Please see examples 2-5. Following, this, a cDNA molecule was identified. Please see example 6 (page 11). It is a murine cDNA molecule. This molecule was then used to identify and isolate genomic DNA. See Example 7. Examples 8 & 9 describe the identification and isolation of additional embodiments. Example 10 confirms the induction of the molecule by IL-9. Example 21 describes how TIF induces STAT activation.

Example 22 describes the identification and isolation of cDNA sequences encoding human TIF. Example 24 describes the isolation of human genomic DNA encoding TIF.

(6) ISSUES

Did the examiner err in rejecting claims 1, 3, 4, 7, 8, 10, 11, 14-16, 18, 19 and 50 under 35 USC §112, first paragraph, as being non-enabled, and deeming the specification enabling for

specific nucleotide sequences only, but not for nucleotide sequences in accordance with the scope of the claims? Appellants claim that the examiner did so err.

(7) GROUPING OF CLAIMS

All of claims 1, 3, 4, 7, 8, 10, 11, 14, 15, 16, 18, 19 and 50 stand or fall together.

(8) ARGUMENT

The claims of the application on appeal are directed to nucleic acid molecules. These nucleic acid molecules must encode a T cell inducible factor, which in turn must activate STAT3, and must also hybridize to one of four different specific sequences, under defined conditions.

The specification explains how the nucleic acid molecules of the invention are expressed in the presence of IL-9, but are not in its absence (page 6 of the specification). Examples 1-6 then describe the isolation of a cDNA molecule (SEQ ID NO: 7), which was found in a sample of IL-9 stimulated murine cells. This molecule (SEQ ID NO: 7), was then used to identify the murine genomic sequence represented by SEQ ID NO: 8.

Following this, a nearly identical murine clone, SEQ ID NO: 9, was identified. Example 8 describes the hight degree of homology between SEQ ID NOS: 7 & 9. As with SEQ ID NO: 7, SEQ ID NO: 9 was then used to identify genomic DNA.

Example 21 describes how both murine and human nucleic acid molecules encoding a form of TIF ("TIFα"), induced STAT activation. Examples 21-23 describe how human cDNA was isolated, and example 24 describes how the human genomic DNA was identified.

SEQ ID NOS: 7, 8, 9, 24, 25 and 29 all correspond to species which are members of the claimed genus. The examiner has not contested this, although she asserts that SEQ ID NOS: 7 and 25 do not constitute part of the claimed invention.

Patent applications are presumed to be enabled. It is the examiner's burden to show, by a preponderance of the evidence, that it would require undue experimentation to practice the claimed invention. If the examiner does not meet this burden, the presumption of enablement is not overcome and the claims should be deemed patentable, should all other criteria for patentability be met.

As the Court stated in In re Marzocchi, 169 USPQ 367, 369 (CCPA. 1971):

> "As a matter of Patent Office practice, then, a specification disclosure which contains a teaching of the manner and process of making the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of §112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied upon for enabling support."

In this case, the examiner does not appear to doubt one could identify nucleic acid molecules which meet the hybridization criteria which are set forth in the claims. Rather, the examiner's argument appears to be that the claimed nucleic acid molecule:

> "can also encompass an indeterminate number and combination of nucleic acid substitutions in SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 24 and SEQ ID NO: 25, by an indefinite number of nucleic acid molecules capable of hybridizing even under stringent hybridization conditions, to a nucleic acid of cDNA and genomic sequences of TIF."

This argument, however, is misplaced because it considers a part of the claimed subject matter, but not all of it. Assuming, arguendo, that there are "an indeterminate number" of nucleic acid molecules which satisfy the criteria of hybridization set forth in the claims, this is not all the molecules must do. Assuming, again arguendo, that there are 250,000 nucleic acid molecules which hybridize to the recited molecules, the claims only embrace those which are T cell inducible factors, which also induce STAT3.

The specification teaches how to determine whether or not a reference molecule induces STAT3 production. See, e.g., example 21. Further, the examples describe how to determine if IL-9 induces expression of the "TIFs." The protocols are laid out completely, and in sufficient detail for one of ordinary skill in the art to determine:

(i) is a particular nucleic acid molecule's expression induced by IL-9?;

(ii) if the answer to (i) is "yes", does the relevant nucleic acid molecule stimulate STAT3 production?;

(iii) if the answer to (ii) is "yes", does the nucleic acid molecule's complementary sequence hybridize under the conditions recited in the claims?

Undoubtedly, determining which nucleic acid molecules satisfy all three criteria requires, experimentation; however, the need for experimentation does not de facto mean undue experimentation.

The examiner's argument that the claims are not enabled is essentially twofold. First, she cites to Doerks, TIG 14(6):248-250 91998), to show, allegedly, that

> "The problem of predicting functional aspects of the product from mere sequence data of a single nucleic acid sequence and what changes can be tolerated is complex and well outside the realm of routine experimentation."

The Doerks paper, however, deals with the issue of assigning function to a protein, based solely on computer data bank information. Applicants are not claiming their invention based on computer generated sequences. Rather, applicants have shown, empirically, how to determine if a given nucleic acid molecule will satisfy the criteria of the claims. Undoubtedly, there are molecules which may satisfy one, or two of the recited criteria, but not all three. Those molecules are not claimed. The examiner seems to be asserting that applicants contend that simply because molecules are structurally related, they will function the same way. Not so. Were this the case, applicants would have felt no need to provide experiments which show that molecules which satisfy structural features of the invention also satisfy the functional features. Applicants do not suggest that one find proteins on the basis of structural similarity only. They suggest testing the molecules.

The examiner then goes on to contend that the unpredictability she asserts is shown by applicants own specification:

> "(W)here it is disclosed on pages 12-14 that the induction by IL-9 of murine TIF beta, which has high homology to murine TIF alpha (and therefore hybridizes to murine TIF alpha under stringent conditions) is much lower than the expression of TIF alpha. Clearly nucleic acid molecules that hybridize under stringent conditions do not necessarily share common functions."

In response, applicants would like to point out that the degree to which the claimed nucleic acid molecules are induced by IL-9, is not a feature recited in the claims, and is thus irrelevant. What pages 12-14 shows is support for what is claimed, since the TIF beta molecule was, in fact induced.

Further, the examiner's argument is contradictory, because while she states that SEQ ID NO: 7 (the nucleic acid molecule in question at pages 12-14), is enabled, she then argues that the very same molecule can be used to show lack of enablement.

The fact is, the molecule identified as SEQ ID NO: 9 was induced by IL-9. Example 8 describes this. Hence, the fact that the molecule is induced by IL-9, regardless of how strong that induction is, is all that the claims require. When one studies the specific members of a genus, there will always be members that are more active than others. This does not mean they are not members of the same genus.

What is ironic about the examiner's position on TIF beta, is that she has taken that position that it constitutes a separate invention and is not to be considered with the present claims! See paper number 9, dated March 26, 2002, Group II in particular. If the subject matter of Group II is not related to the claimed subject matter, then how are its properties relevant to what is claimed? The examiner cannot have it both ways.

The cases cited by the examiner (Amgen, Inc. v. Chugai Pharmaceutical Co. Ltd. 18 USPQ2d. 1016); Ex parte Forman (sic; Formal), 230 USPQ 1924 (CCPA 1970), do not avail her position. In Formal, there was a single embodiment disclosed, with no teachings as to how to find others. Amgen actually deemed broad claims to have satisfied the enablement requirement. In In re Fisher, there wasn't a teaching provided which would permit one to obtain proteins beyond a particular size. Such is not the case here, as the examples evidence the reproducibility of the invention.

The law is very clear that the fact that experimentation is required to practice an invention is acceptable. In re Vaeck, 20 USPQ2d. 1438, 1445 (Fed. Cir. 1991). The issue: is the amount of experimentation required undue? Applicants contend that it is not. The techniques relied upon to reduce the invention to practice are standard, well established procedures, and are clearly set forth in the specification. Working examples are provided, which teach examples of the invention as claimed. All of the claims require the specific properties of the disclosed examples.

The reference relied upon by the examiner (Doerks) does not disclose proteins of the type claimed. It is technology outside of the claims. Ex parte Mark, 12 USPQ2d 1904 (PTO Bd. Pat App & Int. 1989), is relevant, and is believed controlling. Whether the claims are proteins (as in Mark), or nucleic acid molecules (as is the case here), the relevant legal principles remain the same.

The question to be answered is: would one of ordinary skill in the art be enabled to make and use what is claimed? Ex parte Sizto, 9 USPQ2d 2081, 2083 (PTO Bd. Pat App & Int. 1988). As in Sizto, the methodologies needed to practice the invention are routine, and clearly set forth.

Where a specification provides clear and adequate direction to enable one to produce what is claimed, the claims are per se enabled. Ex parte Rinehart, 10 USPQ2d 1719, 1720 (PTO Bd Pat App & Int. 1989).

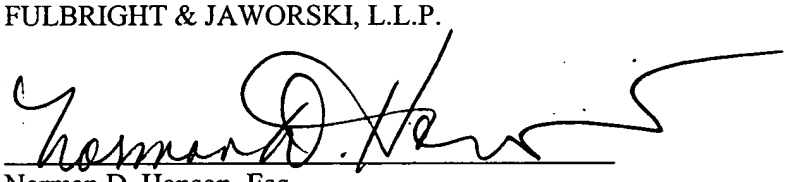
The case of In re Marzocchi is more relevant than any of the cases cited by the examiner. In the absence of the requisite showing, the presumption of enablement has not been overcome, and the rejection is not proper.

(9) CONCLUSION

For the foregoing reasons, it is respectfully requested that the rejection of claims 1, 3, 4, 7, 8, 10, 11, 14-16, 18, 19 and 50 be REVERSED.

Respectfully submitted,

FULBRIGHT & JAWORSKI, L.L.P.



Norman D. Hanson, Esq.
Registration No. 30,946

LISTING OF CLAIMS ON APPEAL

Claim 1: An isolated nucleic acid molecule which encodes a T cell inducible factor which is a protein and which activates STAT3, the complementary sequence of which hybridizes, under stringent conditions defined as 65°C in a 3.5xSSC buffer, 0.02% Ficoll, 0.02% polyvinyl pyrrolidone, 0.02% bovine serum albumin, 25mM NaH_2PO_4 (pH7), 0.1% SDS, 2mM EDTA, followed by a final wash at 2xSSC room temperature, and 0.1xSSC/0.2% SDS at a temperature up to about 65°C, to at least one of SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 24 or SEQ ID NO: 25.

Claim 3: The isolated nucleic acid molecule of claim 1, wherein said molecule is cDNA.

Claim 4: The isolated nucleic acid molecule of claim 1, wherein said molecule is genomic DNA.

Claim 7: An isolated nucleic acid molecule which encodes the protein encoded by the isolated nucleic acid molecule of claim 1.

Claim 8: Expression vector comprising the isolated nucleic acid molecule of claim 1, operably linked to a promoter.

Claim 10: Expression vector comprising the isolated nucleic acid molecule of claim 3, operably linked to a promoter.

Claim 11: Expression vector comprising the isolated nucleic acid molecule of claim 4, operably linked to a promoter.

Claim 14: Recombinant cell comprising the isolated nucleic acid molecule of claim 1.

Claim 15: Recombinant cell comprising the isolated nucleic acid molecule of claim 2.

Claim 16: Recombinant cell comprising the expression vector of claim 8.

Claim 18: Recombinant cell comprising the expression vector of claim 10.

Claim 19: Recombinant cell comprising the expression vector of claim 11.

Claim 50: The isolated nucleic acid molecule of claim 1, wherein said T cell inducible factor which activates STAT 3, has a molecule weight of from about 17 to about 30 kilodaltons, as determined by SDS-PAGE.